Annals of Global Health
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on behalf of Icahn School of Medicine at Mount Sinai

VOL. 81, NO. 5, 2015
ISSN 2214-9996
http://dx.doi.org/10.1016/j.aogh.2015.12.006

ORIGINAL RESEARCH

Alcohol-Attributable Fraction in Liver Disease: Does GDP Per Capita Matter?

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Abstract

BACKGROUND The alcohol-attributable fraction (AAF) quantifies alcohol's disease burden. Alcoholic liver disease (ALD) is influenced by alcohol consumption per capita, duration, gender, ethnicity, and other comorbidities. In this study, we investigated the association between AAF/alcohol-related liver mortality and alcohol consumption per capita, while stratifying to per-capita gross domestic product (GDP).

METHODS Data obtained from the World Health Organization and World Bank for both genders on AAF on liver disease, per-capita alcohol consumption (L/y), and per-capita GDP (USD/y) were used to conduct a cross-sectional study. Countries were classified as "high-income" and "very low income" if their respective per-capita GDP was greater than $30,000 or less than $1,000. Differences in total alcohol consumption per capita and AAF were calculated using a 2-sample *t* test. Scatterplots were generated to supplement the Pearson correlation coefficients, and F test was conducted to assess for differences in variance of ALD between high-income and very low income countries.

FINDINGS Twenty-six and 27 countries met the criteria for high-income and very low income countries, respectively. Alcohol consumption per capita was higher in high-income countries. AAF and alcohol consumption per capita for both genders in high-income and very low income countries had a positive correlation. The F test yielded an F value of 1.44 with $P = .357$. No statistically significant correlation was found among alcohol types and AAF. Significantly higher mortality from ALD was found in very low income countries relative to high-income countries.

DISCUSSION Previous studies had noted a decreased AAF in low-income countries as compared to higher-income countries. However, the non-statistically significant difference between AAF variances of low-income and high-income countries was found by this study. A possible explanation is that both high-income and low-income populations will consume sufficient amount of alcohol, irrespective of its type, enough to weigh into equivalent AAF.

CONCLUSIONS No significant difference of AAF variance was found between high-income and very low income countries relating to sex-specific alcohol consumption per capita. Alcohol consumption per capita was greater in high-income countries. Type of preferred alcohol did not correlate with AAF. ALD related mortality was less in high-income countries as a result of better developed healthcare systems. ALD remains a significant burden globally, requiring prevention from socioeconomic, medical, and political realms.

Preparing this article required no funding of any kind. All authors declare that no conflicts of interest exist. All authors had access to the data, participated in the writing of this manuscript, and agree with its submission.

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Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 711–717

KEY WORDS alcohol-attributable fraction, per capita GDP, liver disease

INTRODUCTION

Excess alcohol consumption worldwide contributes to mortality and morbidity, often leading to injuries, disease, and death, thereby reducing the quality and length of life. The burden of alcohol-related disease (ie, the overall mortality of fatty liver, cirrhosis and its decompensation, and liver cancer) can be measured by the alcohol-attributable fraction (AAF).[1] An excess of 5% of the global disease burden is attributed to alcohol and accounts for nearly 139 million disability-adjusted life years (DALY) and 3.3 million deaths globally.[2] Linking alcohol consumption and health outcomes is multifaceted, often factoring (known to influence the development and progression of liver disease) quantity of alcohol consumed, duration of consumption, beverage type, gender, ethnicity, medical comorbidities (eg, viral hepatitis, genetics, obesity, neuropsychiatric problems), and socioeconomic circumstances.[3] For example, individual studies have also found a positive correlation between alcohol consumption and obesity, smoking, and suicide risk.[4-6] Nonetheless, the per-capita levels of alcohol intake and its influence on mortality related to cirrhosis have endured a strong time-tested relationship across many geopolitical borders, thus allowing for public health efforts to focus on legislation to alter its price and availability.[7] Because the World Health Organization predicts continued increases in alcohol abuse globally, policies to increase taxation and reduce drinking while under the influence of alcohol, availability, and marketing all might be cost effective in reducing alcohol-related harm.[8,9] Moreover, pricing has been a point of debate; because alcohol abusers (particularly in the middle-income levels) tend to buy cheaper alcohol, any legislative price alteration would not affect moderate drinkers, while unfairly targeting the alcohol abusers in the lower-income strata.[10,11]

Although much of the data showing that lower socioeconomic status is a significant risk factor for higher alcohol-related mortality come from high-income countries, there is a lack of generalizable data regarding alcohol-related liver disease (ALD) and income levels globally.[12,13] Mortality from liver disease is unfortunately a common reality, particularly in lower strata of society, partly due to lower access to health care and education, among other factors. However, it fails to take into account the morbidity, an aspect that's hard to quantify and remains a significant portion of the natural history of liver disease progression. Therefore, attributable risk (or fraction) can be used to capture the disease burden accurately. It is the proportion of disease in a population that can be attributable to a certain risk factor (eg, heavy alcohol consumption). Alternatively, it can also be viewed as proportion of disease burden that would be eliminated if the risk/exposure is removed.

In this study, we determined the correlation between alcohol consumption and AAF, while stratifying to per-capita gross domestic product (GDP), in order to investigate ALD across high-income and very low income countries. Additionally, we looked for an association between the types of alcohol used and AAF. Lastly, we plan to reinvestigate alcohol-related mortality caused by liver disease and alcohol consumption, while continuing to stratify by income levels from a population-based perspective.

METHODS

We used available global data from the 2014 World Health Organization (WHO) data on ALD-related mortality and alcohol consumption per capita (in L/y) and from 2014 World Bank database to attain per-capita GDP (in USD/y) in order to conduct a cross-sectional study. Data comprising each of these databases were reported by WHO member states, obtained from their respective national and subnational monitoring systems, and the World Bank economic indicators report of 2014.[2,14] The data are maintained and made available through WHO Global Information System on Alcohol and Health (GISAH).

We used WHO standard definitions for: (1) alcohol per capita consumption, defined as the per-capita amount of alcohol consumed in liters of pure alcohol in a given population, recorded as a 3-year average APC for 2008-2010 and unrecorded

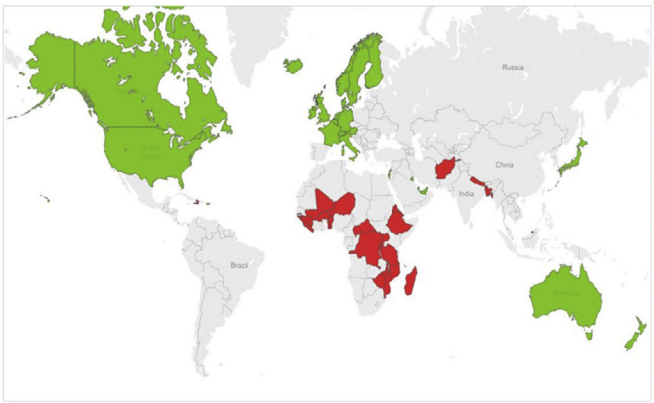
consumption for 2010; (2) types of alcohol, defined as per-capita alcohol consumption in liters of pure alcohol for 2010 for beer, wine, spirits, and other beverages of all recorded per-capita alcohol consumption; (3) age-standardized death, defined as deaths (for each age-sex-disease-country) multiplied by AAF; (4) AAF of liver cirrhosis, defined as a proportion of alcohol-related liver cirrhosis prevented if alcohol is removed and calculated based on level of exposure to alcohol. For sex-specific alcohol consumption data, proportion of alcohol consumed was derived by alcohol consumed by men and women plus the demographics of 2010. Additional information can be found on the WHO website.

Included were countries having a per-capita GDP more than $30,000 USD (defined as "high-income"), and countries having per-capita GDP less than $1,000 USD (defined as "very low income"). Data were obtained for the male and female populations of each country when available. SPSS version 21 statistical software package (IBM Corp., Armonk, NY) was used to interpret the data. Additional information regarding the average population, proportion of population older than 15 years of age, GINI poverty index (which measures the extent of distribution of income or consumption expenditure within an economy), obesity, substance abuse, and suicide risk rates was obtained.

In addition to descriptive analyses, differences in alcohol consumption and alcohol-attributable fraction were calculated using a 2-tailed *t* test for the means between high-income and very low income countries. To visually appreciate if any correlation existed between AAF and alcohol consumption in the 2 cohorts, scatterplots were generated, and the variance and Pearson correlation coefficients were calculated as well. To assess for differences in the 2 categories (high- and very low income countries), the F test for 2 sample variances was used. Second, correlations were calculated between types of alcohol and AAF. Similar analyses were done for alcohol-related mortality as the dependent variable.

RESULTS

Of a total 186 countries, 26 and 27 countries met the study definitions of high-income and very low income countries (median per-capita GDP $50,525 USD and $605 USD), respectively. Characteristics of the countries included are stated in Figure 1. As expected, the high-income countries included tend to be clustered around Western Europe, North America, and Australia, whereas the very low countries are situated in sub-Saharan



Low-Income Countries	(n=27)	High-Income Countries	(n=26)
Afghanistan	Liberia	Australia	Japan
Bangladesh	Madagascar	Austria	Kuwait
Benin	Malawi	Belgium	Luxembourg
Burkina Faso	Mali	Brunei	Netherlands
Burundi	Mozambique	Canada	New Zealand
Cent. African Republic	Nepal	Denmark	Norway
Comoros	Niger	Finland	Qatar
Dem. Rep. Congo	Rwanda	France	Singapore
Eritrea	Sierra Leone	Germany	Sweden
Ethiopia	Togo	Iceland	Switzerland
Gambia	Uganda	Ireland	U.A.E
Guinea	Tanzania	Israel	U.K.
Guinea-Bissau	Zimbabwe	Italy	U.S.A.
Haiti			

Average per capita GDP (USD/year)	$600	$55,775
Average Population	639.6	868.03
Population 15 years or older (%)	59%	82%
Gini Index average	41.2	32.5
Obesity rates (BMI>30)	4.3%	21.2%
Substance abuse in males	1.5%	3.8%
Substance abuse in females	0.2%	1%
Age Std. Suicide rates (per 100000)	11.1	8.9

Figure 1. Characteristics of countries included in the study. Abbreviations: BMI, body mass index.

Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 711–717

Africa. In addition to an older population, the substance abuse and obesity rates were higher in high-income countries relative to the very low income countries; 1%-3.8% versus 0.2%-1.5%, 21.2% versus 4.3%, respectively. Suicide rates were higher in less-affluent countries (11.1%) compared with the affluent countries (8.9%). Although 100% implies perfect inequality regarding income distribution, the GINI index for the countries selected shows lesser income inequality in wealthier countries (32.5%) relative to their less-affluent counterparts (41.2%).

Overall, alcohol consumption per capita was significantly higher in rich countries (mean difference 4.7458, CI 2.1038, $P = .01$) compared with less-affluent countries, for both men and women. A comparison for high-income and low-income countries on per-capita GDP, AAF, alcohol consumption, and cirrhosis mortality is depicted in Table 1. Scatterplots (Figure 2) showed direct correlation between AAF and alcohol consumption per capita separated by sex in high-income and very low income countries. Pearson's correlation coefficients for men in high-income and very low income country were 0.976 and 0.920, respectively, and similar results were seen with women in high-income and very low income countries of 0.951 and 0.875, respectively. In assessing for differences between alcohol consumption in high-income versus very low income countries with sex-specific alcohol consumption, the F test to compare for 2 variances yielded an F value of 1.44 with a P value of .357 (for men). F test to compare alcohol per-capita consumption in women yields a significant increase in high-income countries relative to low-income countries. Additionally, F test to compare AAF for both males and females across different economic circumstances yields P value of 0.587 and 0.757, respectively; thus, we were unable to reject the null hypothesis of being the same.

Comparing the consumption of alcohol (liters of alcohol/year) between affluent and less-affluent countries, the high-income countries tend to drink more beer and wine (3.31 L/y and 2.75 L/d), whereas the lower-income countries tend to drink more of other types of alcohol (1.92 L/y). Correlation coefficients between AAF and beer, wine, and spirits were 0.62, 0.55, and 0.57, respectively, with no statistical significance among them.

The correlation between ALD-related deaths in patients in high-income versus very low income countries and alcohol consumption was calculated, yielding Pearson correlation coefficients of 0.514 and 0.883, respectively. Multiple correlation analysis for this observation yielded a z score of 2.596 and $P = .0049$, indicating a statistically significant difference between the 2 cohorts.

DISCUSSION

In addition to finding a strong positive correlation between alcohol consumption and alcohol-attributable fraction in liver disease, irrespective of gender or per-capita GDP, we present evidence of no significant difference in the per-capita alcohol consumption and AAF between high-income and very low income countries.

AAF and Alcohol Consumption Per Capita. Generally, with greater economic development, more regulated (recorded) alcohol is consumed. According to WHO, high-income countries' unrecorded alcohol consumption only accounted for 8.5%, whereas more

Table 1. Mean, Standard Deviation, and Median for Per-Capita GDP, Alcohol Consumption, Alcohol-Attributable Fraction, and Age-Standardized Cirrhosis Mortality in Male and Female Residents of High-Income and Low-Income Countries

High-Income Countries	Mean	SD	Median	Very Low-Income Countries	Mean	SD	Median
Per-capita GDP (USD)	55776	20000	50525	Per-capita GDP (USD)	600.1	184.3	605
Alcohol consumption in men (L/y)	11.89	5.71	14.5	Alcohol consumption in men (L/y)	6.248	4.722	5.5
Alcohol consumption in women (L/y)	4.815	2.516	5.75	Alcohol consumption in women (L/y)	1.663	1.639	1.1
Total alcohol consumption	8.792	4.588	10.035	Total alcohol consumption	3.903	3.358	3.3
AAF men (%)	54.64	19.6	63.15	AAF men (%)	41.23	22.29	44.7
AAF women (%)	57.12	18.53	65.25	AAF women (%)	42.66	17.77	43.85
Age-standardized cirrhosis mortality in men (number/1000 population)	11.5	6.42	10.55	Age-standardized cirrhosis mortality in men (number/1000 population)	49.98	17.61	50.75
Age-standardized cirrhosis mortality in women	5.565	2.86	5.15	Age-standardized cirrhosis mortality in women	25.43	8.71	23.9

Abbreviations: AAF, alcohol-attributable fraction; GDP, gross domestic product.

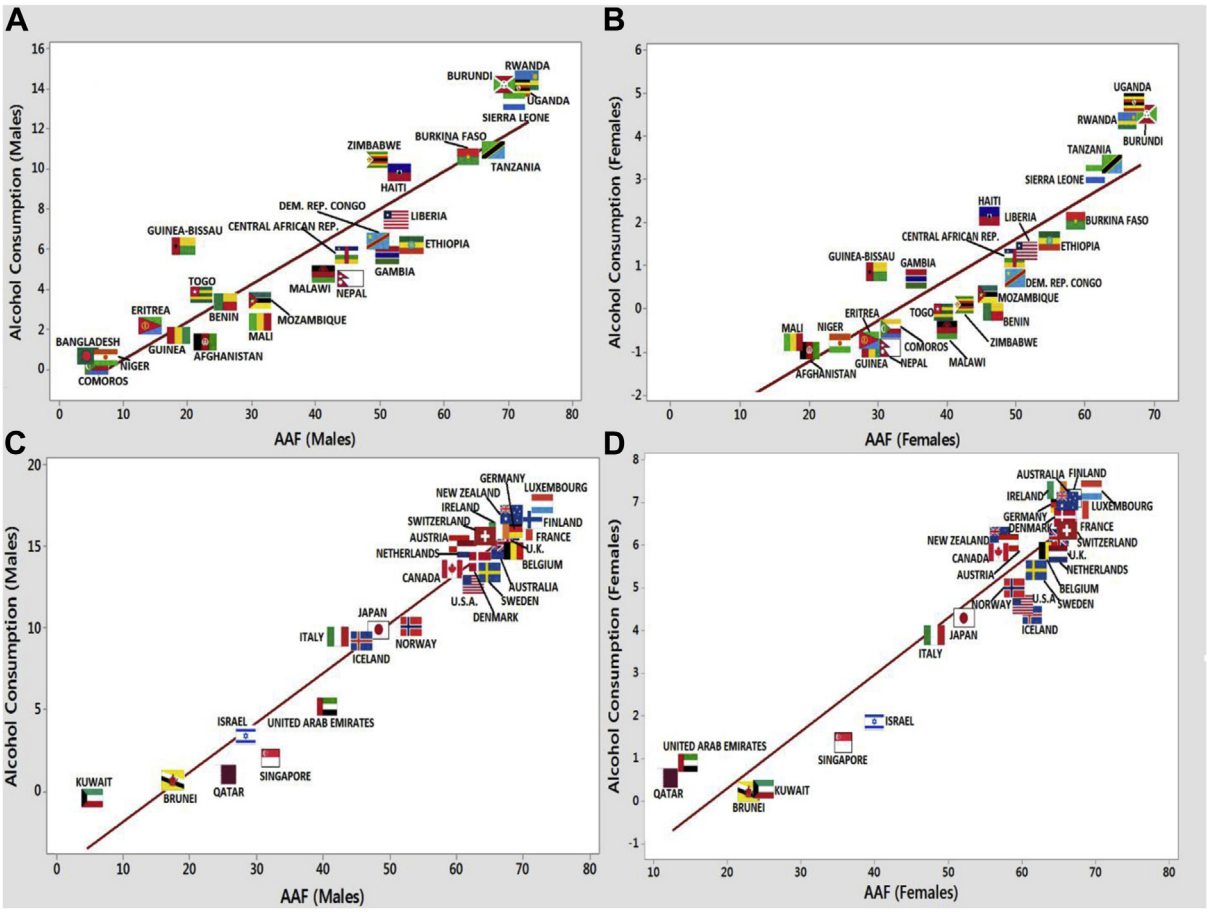


Figure 2. **A linear, positive association can be observed between AAF in males (A, C) and females (B, D) of high-income (C, D) and low-income countries (A, B) alike. Although mostly Western developed nations account for the highest alcohol consumption and AAF, the data are more homogenously distributed on the low-income country graphic. Abbreviations: AAF, alcohol-attributable fraction.**

than 40% of all alcohol consumed in low-income or lower middle income countries is from unrecorded alcohol.[2] This may be a result of cheaper types of alcohol, for which consumption data tend to not be captured by governmental bodies. Yet, consumption of significant amounts of alcohol of any kind can lead to detrimental health consequences, from fatty liver to fibrosis and cirrhosis, and even to hepatocellular carcinoma. Moreover, continued use of alcohol, in addition to underlying hepatitis infection, proves to be synergistic in the disease progression and may lead to decompensation.[15,16] Nevertheless, alcohol plays an important role in the development and progression of liver disease, transcending geopolitical and economic boundaries.[17] For example, 47.9% of total burden of liver cirrhosis deaths were attributable to alcohol intake, including 46.5% for women and 48.5% for men. Yet, the high burden is entirely preventable.

Although liver disease mortality data provide us with a glimpse into a definite point in the natural history of liver disease, alcohol-attributable fraction, however, provides us with information regarding the global burden of the disease. The risk of alcohol-related liver disease can be measured with AAF, depending on the level of exposure. Studies mention that lower-income countries typically have lower AAF compared with higher-income countries, which is likely a result of increased mortality rates in these lower-income countries. However, the observations of this study support the fact that no statistically significant difference in AAF exists between countries of high and low GDP per capita.[1] Pearson correlation values obtained for male and

Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 711–717

female populations did not statistically differ significantly, supporting the claim that gender also does not play a role. Moreover, AAF has been used to investigate alcohol-related injuries in emergency department visits in 18 countries, showing that 16.4% of all injuries were likely due to alcohol, irrespective of age, with men being affected twice as much as their female counterparts.[18]

AAF and Types of Alcohol. In addition to the different levels of consumption globally depending on region, the most consumed beverage type in the world is in the form of spirits, and beer accounts for the second most common beverage. The possible reasons could include a shift in consumed beverages to less regulated and unrecorded types as a result of ease of accessibility and economics.[19] The variations also extend to consumption patterns as well. These variations are part of complex interacting factors that range from economic development, culture, and religion to social norms and individual preference. Nevertheless, the studies investigating types of alcohol consumed have consistently shown a J-shaped relationship between alcohol and all-cause mortality, with a relative risk of 0.82 in people drinking 1 to 10 drinks weekly and a relative risk of 1.10 for people who consumed more than 35 drinks weekly.[20,21] Investigating types of alcohol (ie, beer, wine, and spirits) has led to some evidence to support that moderate intake of wine may be protective, though fewer signs point to a certain type of alcohol (not amount) leading to alcohol-related liver disease.[22] As observed in this study, type of preferred alcohol did not play a role in AAF. This relationship of alcohol (regardless of type) and liver disease may not be limited to population medicine, but may also include communities and individuals.

ALD-related Mortality and Alcohol Consumption Per Capita. Although the consumption of alcohol is significantly higher in higher-income countries, alcohol-attributed mortality has been found to be lower.[2] The main difference observed was in terms of ALD-related mortality, in which the favorable difference for the high-income countries may be on account of improved access to the healthcare system, leading to improved management and treatment of ALD complications and better outcomes. This has been evidenced by increasing the rate of treatment of alcohol-related disorders with a resulting decrease in the mortality burden of alcohol-attributed diseases. Additionally, alcohol is related to all injuries, particularly those that are violence related.

Limitations. Although data were obtained through the WHO database, some are incomplete because of the poorly kept statistics in very low income countries, which may influence the results. Another problem is that the use of onetime measurements of alcohol intake may not be representative of the cumulative chronic effect of exposure in alcohol liver disease; besides, it could easily be under-reporting as a result of several socioeconomic and cultural factors that could affect the accuracy of the data.

CONCLUSIONS

No significant difference of AAF variance was found between high-income and very low income countries in relation to sex-specific alcohol consumption. The consumption of alcohol is significantly greater in high-income countries. No difference between type of preferred alcohol ingested and AAF was observed, for which only the quantity of alcohol consumed shows a direct relation with AAF. ALD-related mortality was significantly lower in high-income countries, likely owing mainly to the fact that higher-income countries have better developed healthcare systems to treat ALD and its complications. Nonetheless, alcoholic liver disease is a huge burden on the global level and requires primary and secondary prevention from the socioeconomic, medical, and political realms.

REFERENCES

1. Rehm J, Shield KD. Alcohol and mortality: global alcohol-attributable deaths from cancer, liver cirrhosis, and injury in 2010. Alcohol Res Curr Rev 2014;35:174–83.
2. World Health Organization. Global status report on alcohol and health 2014. Geneva, Switzerland: WHO; 2014. Contract No.: ndc:21884.
3. O'Shea RS, Dasarathy S, McCullough AJ. Alcoholic liver disease. Hepatology (Baltimore) 2010;51:307–28.
4. Darvishi N, Farhadi M, Haghtalab T, Poorolajal J. Alcohol-related risk of suicidal ideation, suicide attempt, and completed suicide: a meta-analysis. PloS One 2015;10:e0126870.
5. Suter PM. Is alcohol consumption a risk factor for weight gain and obesity? Crit Rev Clin Lab Sci 2005;42:197–227.

6. De Leon J, Rendon DM, Baca-Garcia E, et al. Association between smoking and alcohol use in the general population: stable and unstable odds ratios across two years in two different countries. Alcohol Alcoholism (Oxford) 2007;42:252–7.
7. Mann RE, Smart RG, Govoni R. The epidemiology of alcoholic liver disease. Alcohol Res Health 2003;27:209–19.
8. Anderson P, Chisholm D, Fuhr DC. Effectiveness and cost-effectiveness of policies and programmes to reduce the harm caused by alcohol. Lancet 2009;373:2234–46.
9. Chisholm D, Rehm J, Van Ommeren M, Monteiro M. Reducing the global burden of hazardous alcohol use: a comparative cost-effectiveness analysis. J Studies Alcohol 2004;65: 782–93.
10. Ludbrook A, Petrie D, McKenzie L, Farrar S. Tackling alcohol misuse: purchasing patterns affected by minimum pricing for alcohol. Appl Health Econ Health Pol 2012;10:51–63.
11. Holmes J, Meng Y, Meier PS, et al. Effects of minimum unit pricing for alcohol on different income and socioeconomic groups: a modelling study. Lancet 2014;383(9929): 1655–64.
12. Probst C, Roerecke M, Behrendt S, Rehm J. Gender differences in socioeconomic inequality of alcohol-attributable mortality: A systematic review and meta-analysis. Drug Alcohol Rev 2015;34(3):267–77.
13. Probst C, Roerecke M, Behrendt S, Rehm J. Socioeconomic differences in alcohol-attributable mortality compared with all-cause mortality: a systematic review and meta-analysis. Int J Epidemiol 2014;43: 1314–27.
14. Bank W. World Development Indicators 2014. Washington, DC: World Bank; 2014.
15. Mankal PK, Abed J, Aristy JD, et al. Relative effects of heavy alcohol use and hepatitis C in decompensated chronic liver disease in a hospital inpatient population. Am J Drug Alcohol Abuse 2015;41:177–82.
16. Frieden TR, Ozick L, McCord C, et al. Chronic liver disease in central Harlem: the role of alcohol and viral hepatitis. Hepatology (Baltimore) 1999;29:883–8.
17. Rehm J, Taylor B, Mohapatra S, et al. Alcohol as a risk factor for liver cirrhosis: a systematic review and meta-analysis. Drug Alcohol Rev 2010;29: 437–45.
18. Cherpitel CJ, Ye Y, Bond J, et al. Alcohol attributable fraction for injury morbidity from the dose-response relationship of acute alcohol consumption: emergency department data from 18 countries. Addiction 2015;110: 1724–32.
19. Medina-Mora ME. An alternative taxation method for low- to middle-income countries. Addiction 2012;107:1386–7.
20. Grønbæk M, Becker U, Johansen D, et al. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. Ann Intern Med 2000;133:411–9.
21. Fuchs CS, Stampfer MJ, Colditz GA, et al. Alcohol consumption and mortality among women. N Engl J Med 1995;332:1245–50.
22. Gronbaek M, Jensen MK, Johansen D, Sorensen TI, Becker U. Intake of beer, wine and spirits and risk of heavy drinking and alcoholic cirrhosis. Biol Res 2004;37: 195–200.